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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,440	10/01/2003	Gregor Sagner	21428-US	1058

22829 7590 10/22/2007

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EXAMINER	
POHNERT, STEVEN C	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
10/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/678,440	SAGNER ET AL.	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *8-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/22/2004, 4/2/2004, 2/5/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of group I, claims 1-7 in the reply filed on 7/31/2007 is acknowledged.

2. Claims 8-12 have withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/31/2007.

Information Disclosure Statement

3. The information disclosure filed on 2/5/2007 lists JP62-240864, JP7-502992, JP10-88124 and JP 9-5085525. JP62-240864, JP7-502992, JP10-88124 and JP 9-5085525 have been provided, however the provided references are not in English and thus have not been considered.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 2, 4, 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 and dependent claims 6 and 7 are drawn to a pair of FRET hybridization probes. However, claim 1 requires a single nucleic acid sequence with a FRET donor or a FRET acceptor. FRET requires the presence of a donor and acceptor molecule, it is thus unclear how a single nucleic acid with either a donor or acceptor

would comprise a FRET pair. Further the claim is drawn to a pair of probes, but only requires a single nucleic acid. It is thus unclear how this is a pair.

Claim 4 recites, "spacer entity comprising a number of n=1-15 nucleotides," however the specification teaches "the term "spacer entity" comprises all items between the fluorescent chromophore which are not participating in mesomeric effects and on the other side all items which are not apart of the ribose entity of either the 5' or 3' terminal nucleotide." It is thus unclear how the spacer entity comprises nucleotides, as the specifications definition of "spacer entity" is referring to the 5' or 3' terminal nucleotide of the sequence that is base pairing with the target sequence?

6. Claim 6 recites the limitation "a pair of hybridization probes according to any of claims 1 to 5". There is insufficient antecedent basis for this limitation in the claim as claim 5 is drawn to a set of at least three oligonucleotides.

7. Claims 6 recites, "a pair of hybridization probes according to any of claims 1 to 5" although claims 1-4 refer to a pair of FRET hybridization probes. IT is thus unclear which probes are being referred to.

8. Claim 7 recites the limitation "hybridization probes according to any of claims 1 to 5". There is insufficient antecedent basis for this limitation in the claim as claim 5 is drawn to a set of at least three oligonucleotides.

9. Claims 7 recites, "hybridization probes according to any of claims 1 to 5" although claims 1-4 refer to a pair of FRET hybridization probes. IT is thus unclear which probes are being referred to.

Claim Rejections - 35 USC § 102

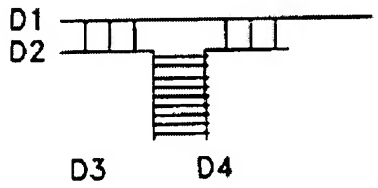
10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Nadeau et al (US patent 6,130,047 issued October 10, 2000).

The spacer entity is being broadly interpreted as nucleic acids of the probes.

With regards to claim 1, Nadeau teaches the in figure 3,



Nadeau teaches this figure represents a nucleic acid labeled with energy transfer pairs (donor and acceptor). The hatch marks represent nucleic acid's base pairing. The FRET entities are attached to nucleotides that comprise at least 15 atoms and the oxygens of the phosphodiester bond are negatively charged. Nadeau thus teaches a FRET hybridization probe pair (D2D3 and D4) hybridizing adjacently to a target nucleic acid sequence (D1), a spacer entity (the hybridized nucleic acids between D3 and D4) comprising at least 15 atoms with 2 atoms of said connecting region being negatively charged.

Claim 2 is drawn to a spacer comprising between 1-10 A, T, or C residues that are not complementary to the target nucleic acid. As the spacer region comprises A, T, or C it is not limited to these residues and thus comprises any nucleic acid with 1-10 A, T, or C residues, and thus could require a single nucleotide spacer or a spacer of any number of nucleotides as long as it contains no more than 10 A, 10 T, or 10 C. Further the claims are comprising language so the spacer region can be longer than 10 nucleotides if the claim is viewed to limit the spacer region to 10 nucleotides total, or longer than 30 nucleotides if the claims are interpreted to be drawn to 10 A, 10T and 10C.

With regards to claim 2, Nadeau teaches the spacer region with basepairing between D3 and D4 is 9 nucleic acids. Nadeau thus teaches a spacer region comprising 1-10 A, T, or C residues.

With regards to claim 3, Nadeau teaches Figure 3 as depicted above. Probes D1 and D2D3 hybridized to target nucleic D4. Probes D1 and D2D3 comprise a FRET energy transfer pairs (FRET donor entity and FRET acceptor entity). As D1 is longer than D2D3 the length of the first spacer entity and the second spacer entity differ in size by at least 15 atoms.

Claim 4 comprises a spacer entity with length n1 and a second spacer entity of length n2 and that n1 and n2 differ by a natural number between 1 and 10. The probes D1 and D2D3 of Nadeau are probe pairs that bind target DNA sequence D4. D1 comprises nucleic acids and is longer than D2D3. The nucleotides of D1 and D2D3 are the spacer entity comprise a FRET pair with different length spacer, and as the

language is comprising would inherently have different number of nucleotides and could be defined in such a way that the differ by between 1 and 10 nucleotides.

With regards to claim 5, Nadeua teaches in figure 3, fluorescently labeled probes D1, D2D3 and D4. The probes are labeled with FRET energy transfer pairs and thus consist of donor and acceptor entities. As D1, D2D3 and D4 are made of nucleic acids, they are capable of acting as primers for template dependent amplification reaction. D1 is complementary to the target nucleic acid and is longer than D2D3 or D4 and thus comprises a connecting chain of at lest 15 atoms.

With regards to claim 6, Nadeau teaches in figure 3 a target nucleic acid and probe D1, D2D3 and D4. Nadeua thus teaches a composition accrding to claims 1-5.

Claim Rejections - 35 USC § 103

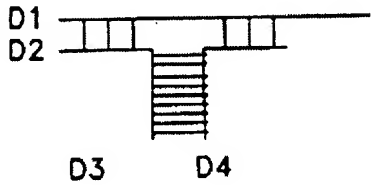
12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nadeau et al (US patent 6,130,047 issued October 10, 2000) in view Ahern et al (The Scientist (1995) volume 9 page 1-7).

The spacer entity is being broadly interpreted as nucleic acids of the probes.

Nadeau teaches the in figure 3,



Nadeau teaches this figure represents a nucleic acid labeled with energy transfer pairs (donor and acceptor). The hatch marks represent nucleic acid's base pairing. The FRET entities are attached to nucleotides that comprise at least 15 atoms and the oxygens of the phosphodiester bond are negatively charged. Nadeau thus teaches a fret hybridization probe pair (D2D3 and D4) hybridizing adjacently to a target nucleic acid sequence (D1), a spacer entity (the hybridized nucleic acids between D3 and D4) comprising at least 15 atoms with 2 atoms of said connecting region being negatively charged. Nadeau teaches a reactions mixture comprising probes, a nucleic acid polymerase, deoxynucleotide triphosphates and buffer for mucleic acid amplification (see column 17, lines 19-23).

Nadeau does not teach kits.

However, Ahern teaches kits containing all biochemical reagents needed to perform assays are often used in research as they are convenient and save time (see page 5, 1st full paragraph).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine all the reagents that Nadeau teaches are necessary for his FRET probe based assay in a kit as taught by Ahern. The ordinary artisan would be motivated to combine the reagents of Nadeau in the kit of Ahern because Ahern teaches kits are more time efficient and convenient.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1-7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 38 and 39 of copending Application No. 10/621428. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 1 of instant invention is drawn to FRET hybridization probes containing a nucleotide sequence entity, a FRET donor or FRET acceptor and a spacer entity. Claim 1 of '428 is drawn to a plurality of FRET hybridization probes comprising a nucleotide and a FRET donor and acceptor entity. Although claim 1 of '428 does not

specifically recite the nucleotide to which a spacer entity is attached is 15 atoms and has 2 negative charges. Claim 1 of instant invention is thus obvious over claim 1 of '428.

Claim 3 of instant application is drawn to FRET hybridization probes containing a first nucleotide sequence entity, a FRET donor and spacer entity and a second nucleotide sequence, a fluorescent acceptor entity, and a spacer entity. Claim 1 of '428 is drawn to a plurality of FRET hybridization probes comprising a nucleotide and a FRET donor and acceptor entity, where the first oligonucleotide comprises an donor entity and the second oligonucleotide has an acceptor entity. Claim 3 of instant invention is thus obvious over claim 1 of '428.

Claim 5 of instant claims requires a first oligonucleotide and a second oligonucleotide, said first oligonucleotide and said second oligonucleotide being capable of acting as a pair of amplification primers for a template dependent nucleic acid amplification reaction, each of said first oligonucleotide and said third oligonucleotide being labeled with one corresponding member of a FRET pair consisting of a FRET donor entity and a FRET acceptor entity; one of said first said oligonucleotide or said third oligonucleotide comprising: a nucleotide sequence entity which is substantially complementary to the sequence of the target nucleic acid; a fluorescent entity, said entity being either the FRET donor entity or the FRET acceptor entity; a spacer entity connecting said nucleotide sequence entity and said fluorescent entity; wherein said spacer entity comprises a connecting chain of at least 15 atoms. Claim 35 or '428 teaches A set of 3 oligonucleotides, comprising a first oligonucleotide and a

second oligonucleotide capable of acting as a pair of amplification primers for a template dependent nucleic acid amplification reaction, further characterized in that said first oligonucleotide and a third oligonucleotide are each labeled with one corresponding member of a FRET pair consisting of a FRET donor entity and a FRET acceptor entity, wherein the oligonucleotide carrying the FRET donor entity is carrying a nitroindole moiety capable of quenching fluorescence of said FRET donor entity.. Thus instant claim 1 is anticpaited by claim 35 of '428.

Claim 6 of instant invention is drawn to A composition comprising a nucleic acid sample and a pair of hybridization probes according to any of Claims 1-5. Claim 38 of '428 is drawn to composition comprising a nucleic acid sample and a pair of hybridization probes according to claim 33 or a set of oligonucleotides according to claim 35. Claim 6 of instant application is obvous over claim 38 of '428.

Instant claim 7 is drawn to a kit comprising hybridization probes according to any of Claims 1-5 and at least one other component selected from a group consisting of nucleic acid amplification primers, template dependent nucleic acid polymerase, deoxynucleoside triphosphates and a buffer for template dependent nucleic acid amplification reaction. Claim 39 of '428 is drawn to A kit comprising a pair of hybridization probes according to claim 33 or a set of oligonucleotides according to claim 35 and at least one other component selected from a group consisting of a nucleic acid amplification primer a template dependent nucleic acid polymerase, at least one deoxynucleoside triphosphate and a buffer for template dependent nucleic acid amplification reaction.

15. Claims 1-7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/549,648. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are co-extensive in scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3, and 5 of instant invention are drawn to FRET hybridization probes containing a nucleotide sequence entity, a FRET donor or FRET acceptor and a spacer entity. Claim 1 of '648 teaches composition or reaction mixture for performing multi-color real time PCR comprising at least 3 pairs, of FRET hybridization probes, each pair of hybridization probes consisting of a FRET donor probe carrying a FRET donor moiety and a FRET acceptor probe carrying a FRET acceptor moiety.

Claims 3 and 5 of instant specification are drawn to hybridization probes having spacer of nucleotides of different lengths. Claim 1 teaches the concept of FRET hybridization probes while paragraph 0116 teaches the use of probes differing by additions or deletions of nucleotides. Thus claims 3 and 5 are obvious in view of claim 1 of '648 and the specification of '648.

Instant claims 6 and 7 are drawn to a kit comprising hybridization probes according to any of Claims 1-5 and at least one other component selected from a group consisting of nucleic acid amplification primers, template dependent nucleic acid polymerase, deoxynucleoside triphosphates and a buffer for template dependent nucleic acid amplification reaction. The specification of '648 teaches a kit (see

paragraph 0155). Thus instant claim 7 is obvious over claim 1 of '648 and its specification.

Summary

No claims are allowed over prior art cited.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

/Carla Myers/
Primary Examiner, Art Unit 1634